CLAIMS

1. An isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less.

2. The isolated human antibody, or antigen-binding portion thereof, of claim 1, which dissociates from human TNFα with a K_{off} rate constant of 5 x 10^{-4} s^{-1} or less, .

3. The isolated human antibody, or antigen-binding portion thereof, of claim 1, which dissociates from human TNFα with a K_{off} rate constant of 1 x 10^{-4} s^{-1} or less.

4. The isolated human antibody, or antigen-binding portion thereof, of claim 1, which neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-8} M or less.

5. The isolated human antibody, or antigen-binding portion thereof, of claim 1, which neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-9} M or less.

6. The isolated human antibody, or antigen-binding portion thereof, of claim 1, which neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 5 x 10^{-10} M or less.

7. The isolated human antibody, or antigen-binding portion thereof, of claim 1, which is a recombinant antibody, or antigen-binding portion thereof.

8. The isolated human antibody, or antigen-binding portion thereof, of claim 1, which inhibits human TNFα-induced expression of ELAM-1 on human umbilical vein endothelial cells.

9. An isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

10. The isolated human antibody of claim 9, or an antigen-binding portion thereof, which dissociates from human TNFα with a K_{off} rate constant of 5 x 10^{-4} s^{-1} or less.

11. The isolated human antibody of claim 9, or an antigen-binding portion thereof, which dissociates from human TNFα with a K_{off} rate constant of 1 x 10^{-4} s^{-1} or less.

12. An isolated human antibody, or an antigen-binding portion thereof, with a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8, and with a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11.

13. The isolated human antibody, or an antigen-binding portion thereof, of claim 12, wherein the LCVR further has a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 5 and the HCVR further has a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 6.

14. The isolated human antibody, or an antigen-binding portion thereof, of claim 13, wherein the LCVR further has CDR1 domain comprising the amino acid sequence of SEQ ID NO: 7 and the HCVR has a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 8.

15. An isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

16. The isolated human antibody of claim 15, which has an IgG1 heavy chain constant region.

17. The isolated human antibody of claim 15, which has an IgG4 heavy chain constant region.

18. The isolated human antibody of claim 15, which is a Fab fragment.

19. The isolated human antibody of claim 15, which is a single chain Fv fragment.

20. An isolated human antibody, or an antigen-binding portions thereof, with a light chain variable region (LCVR) having a CDR3 domain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26 or with a heavy chain variable region (HCVR) having a CDR3 domain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 4, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33 and SEQ ID NO: 34.

21. A recombinant human antibody, or antigen-binding portion thereof, that neutralizes the activity of human TNFα but not human TNFβ.

22. The recombinant human antibody, or antigen-binding portion thereof, of claim 21, which also neutralizes the activity of chimpanzee TNFα and at least one additional primate TNFα selected from the group consisting of baboon TNFα, marmoset TNFα, cynomolgus TNFα and rhesus TNFα.

23. The recombinant human antibody, or an antigen-binding portion thereof, of claim 22, which also neutralizes the activity of canine TNFα.

24. The recombinant human antibody, or an antigen-binding portion thereof, of claim 22, which also neutralizes the activity of pig TNFα.

25. An isolated nucleic acid encoding a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8, or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9.

26. The isolated nucleic acid of claim 25, which encodes an antibody light chain variable region (LCVR).

27. The isolated nucleic acid of claim 26, wherein the CDR2 domain of the antibody LCVR comprises the amino acid sequence of SEQ ID NO: 5.

28. The isolated nucleic acid of claim 27, wherein the CDR1 domain of the antibody LCVR comprises the amino acid sequence of SEQ ID NO: 7.

29. An isolated nucleic acid encoding a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11, or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

30. The isolated nucleic acid of claim 29, which encodes an antibody heavy chain variable region (HCVR).

31. The isolated nucleic acid of claim 30, wherein the CDR2 domain of the antibody HCVR comprises the amino acid sequence of SEQ ID NO: 6.

32. The isolated nucleic acid of claim 31, wherein the CDR1 domain of the antibody HCVR comprises the amino acid sequence of SEQ ID NO: 8.

33. An isolated nucleic acid encoding a CDR3 domain comprising an amino acid sequence selected from the group consisting of: SEQ ID NO: 3, SEQ ID NO 4,

SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33 and SEQ ID NO: 34.

34. An isolated nucleic acid encoding an antibody light chain variable region comprising the amino acid sequence of SEQ ID NO: 1.

35. The isolated nucleic acid of claim 34, which encodes the antibody light chain variable region and an antibody light chain constant region.

36. The isolated nucleic acid of claim 35, which is in a recombinant expression vector.

37. An isolated nucleic acid encoding an antibody heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 2.

38. The isolated nucleic acid of claim 37, which encodes the antibody heavy chain variable region and an antibody heavy chain constant region.

39. The isolated nucleic acid of claim 38, wherein the antibody heavy chain constant region is an IgG1 constant region.

40. The isolated nucleic acid of claim 38, wherein the antibody heavy chain constant region is an IgG4 constant region.

41. The isolated nucleic acid of claim 38, which is in a recombinant expression vector.

42. A recombinant expression vector encoding:

a) an antibody light chain having a variable region comprising the amino acid sequence of SEQ ID NO: 1; and

b) an antibody heavy chain having a variable region comprising the amino acid sequence of SEQ ID NO: 2.

43. A host cell into which the recombinant expression vector of claim 42 has been introduced.

44. A method of synthesizing a human antibody that binds human TNFα, comprising culturing the host cell of claim 43 in a culture medium until a human antibody that binds human TNFα is synthesized by the cell.

45. A pharmaceutical composition comprising the antibody, or antigen-binding portion thereof, of any of claims 1-24, and a pharmaceutically acceptable carrier.

46. The pharmaceutical composition of claim 45, which further comprises at least one additional therapeutic agent for treating a disorder in which TNFα activity is detrimental.

47. A method for inhibiting human TNFα activity comprising contacting human TNFα with the antibody, or antigen-binding portion thereof, of any of claims 1-24 such that human TNFα activity is inhibited.

48. A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the human subject the antibody, or antigen-binding portion thereof, of any of claims 1-24 such that human TNFα activity in the human subject is inhibited.

49. The method of claim 48, wherein the disorder is sepsis.

50. The method of claim 49, wherein the antibody is administered to the human subject together with the cytokine interleukin-6 (IL-6) or is administered to a human subject with a serum or plasma concentration of IL-6 above 500 pg/ml.

51. The method of claim 48, wherein the disorder is an autoimmune disease.

52. The method of claim 51, wherein the autoimmune disease is selected from the group consisting of rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis and gouty arthritis.

53. The method of claim 51, wherein the autoimmune disease is selected from the group consisting of an allergy, multiple sclerosis, autoimmune diabetes, autoimmune uveitis and nephrotic syndrome.

54. The method of claim 48, wherein the disorder is an infectious disease.

55. The method of claim 48, wherein the disorder is transplant rejection or graft-versus-host disease.

56. The method of claim 48, wherein the disorder is a malignancy.

57. The method of claim 48, wherein the disorder is a pulmonary disorder.

58. The method of claim 48, wherein the disorder is an intestinal disorder.

59. The method of claim 48, wherein the disorder is a cardiac disorder.

60. The method of claim 48, wherein the disorder is selected from the group consisting of inflammatory bone disorders, bone resorption disease, alcoholic hepatitis, viral hepatitis, fulminant hepatitis, coagulation disturbances, burns, reperfusion injury, keloid formation, scar tissue formation, pyrexia, periodontal disease, obesity and radiation toxicity.

61. Use of the antibody, or antigen-binding portion thereof, of any of claims 1-24 in the manufacture of a medicament for the treatment of a a disorder in which TNFα activity is detrimental.

62. The use of claim 61, wherein the disorder is sepsis.

63. The use of claim 62, wherein the antibody is administered to the human subject together with the cytokine interleukin-6 (IL-6) or is administered to a human subject with a serum or plasma concentration of IL-6 above 500 pg/ml.

64. The use of claim 61, wherein the disorder is an autoimmune disease.

65. The use of claim 64, wherein the autoimmune disease is selected from the group consisting of rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis and gouty arthritis.

66. The use of claim 64, wherein the autoimmune disease is selected from the group consisting of an allergy, multiple sclerosis, autoimmune diabetes, autoimmune uveitis and nephrotic syndrome.

67. The use of claim 61, wherein the disorder is an infectious disease.

68. The use of claim 61, wherein the disorder is transplant rejection or graft-versus-host disease.

69. The use of claim 61, wherein the disorder is a malignancy.

70. The use of claim 61, wherein the disorder is a pulmonary disorder.

71. The use of claim 61, wherein the disorder is an intestinal disorder.

72. The use of claim 61, wherein the disorder is a cardiac disorder.

73. The use of claim 61, wherein the disorder is selected from the group consisting of inflammatory bone disorders, bone resorption disease, alcoholic hepatitis, viral hepatitis, fulminant hepatitis, coagulation disturbances, burns, reperfusion injury, keloid formation, scar tissue formation, pyrexia, periodontal disease, obesity and radiation toxicity.